REMARKS

1. According to the Office Communication, the applicants have amended the claim 33 to improve the grammar of the claim as the examiner indicated.
2. Regarding the new rejection citing Caplan et al. US 5811094 patent, the applicants have further amended claim 1 by adding the "culturing" limitation. As mentioned in the specification of this application, "after seeding bone marrow cells ..., and non-adherent cells can be removed by following changes of medium. ... , and reach confluence at 17 days later following the first seeding." [0029] [0034] also disclosed that " the cultures were maintained at 37℃ in 5% CO_2 in air, with medium changes first at 7 days after initial plating and then every 4 days." Therefore, the limitation added will not bring a new matter issue.
3. In the US Patent No. 5811094, Caplan et al seed the cell mixture in a Leukosorb™ filter, which fat and red blood cells pass through and fat and red blood cell-deleted cell mixture retain, and then recover the remained cell mixture by elution. The 5811094 patent did not culture the cell mixture in a Leukosorb™ filter. Furthermore, the Patent of Caplan et al, requiring the elute of the remained cell mixture prior culturing, teaches away from the invention of this application, which uses the device to culture cells. The request of further elution prior culturing is consistent with the purpose of Leukosorb™ filter, which is used for filtering and not for culturing. In general, the culture procedures include seeding the cells in a culture device and maintaining the cells in the device for several days to several weeks in an incubator which provides temperature and atmosphere controls.

   Besides, as mentioned in Page 5, Line12-15, Caplan et al do not specially teach culturing the mesenchymal stem cells recovered from the Leukosorb™ filter in 10% fetal bovine serum-supplemented Dulbecco's modified Eagle's medium containing 1 g/L glucose. Meanwhile, the mesenchymal stem cells

prepared as described above are still not ready for use. Therefore, Caplan et al teach further enriched by passage over an hydroxyapatite column and by monoclonal antibody separation (column 46, lines 11-61).

4. In the US Patent No. 5824084, Muschler et al. do not teach method for recovering mesenchymal stem cells from human bone marrow aspirate or a cell mixture. On the other hand, Muschler et al teach a method for preparing a composite bone graft, which includes providing a bone marrow aspirate suspension and passing the bone marrow aspirate suspension through a porous, biocompatible, implantable substrate (column 3, lines 31-38) to provide a composite bone graft for use intraoperatively (column 2, lines 14-29).

   In comparison with this application, Muschler et al specifically indicate the plate for cell attachment, which is made of biocompatible and implantable substrate, upon which cells are loaded and used for grafting together. In other words, cells are not recovered from the plate in the patent of Muschler et al. Furthermore, the plate of this application is made of plastic or glass for mesenchymal stem cells adherence. In shorts, Caplan et al. teach away from this application as well as the way and result of Muschler et al are different from this application. Therefore, a person in the art certainly will not be obvious to combine Caplan's and Muschler's patents to be this invention of this application.

5. In the Us Patent No. 6242247 B1, Rieser et al. do not teach method for recovering mesenchymal stem cells from human bone marrow aspirate or a cell mixture. On the other hand, Rieser et al teach a method for preparing a cell-contained graft, which includes providing a cell mixture comprising cells having the ability to form an extracellular cartilage matrix and introducing the cells to a cell space (1), which is at least partly separated from a culture medium space (2) surrounding the

cell space by a semi-permeable wall (3) or by an open-pore wall acting as convection barrier (column 4, lines 29-35, column 5, lines 56-67). Reiser et al mainly indicate that the open-pore wall can be designed as a plate (7) made of a bone substitute material. As bone substitute material, known osteo-inductive and/or osteo-conductive materials are suitable, advantageously biologically degradable such materials which have the mentioned open porosity and which can be processed to rigid or plastically deformable plates. Plastically deformable plates can e.g. be produced from collagen I, from collagen II and hydroxyapatite or from poly-lactic acid. Rigid plates can be formed from tricalcium-phosphate, from hydroxyapatite or from other inorganic bone substitute materials (Column 8. lines 17-25). Furthermore, the bone substitute plate (7) must be formed such that the cartilage tissue is able to grow within the bone substitute and be implanted with the plate (7) together (cells are not recovered from the wall). Especially, the pore size in the bone substitute plate (7) should be optimized that the cartilage fibrils built in the extracellular cartilage matrix can grow into the pores and can such anchor the new cartilage in the bone substitute plate (column 7, lines 35-45).

Reiser et al teach a method for preparing a cell-contained graft by optimizing the bone substitute plate and the culture medium to let the chondrocyte remains active and do not de-differentiate. In short, the plate with pores in Rieser et al is for cell growth but not a filter. However, the upper plate with pores in this application is to separate mesenchymal stem cells from other cells. The functions of Rieser et al and this application are different, even though the pore sizes are similar. Therefore, it would not have been obvious to one of ordinary skill in the art at the time of this invention to modify the method of isolating mesenchymal stem cells of Caplan et al (teach away from this

application as mentioned above) to include the introduction of bone marrow into the cell space and culture dish taught by Rieser et al (the functions are different).

6. The new rejection cited three patents of Caplan et al, Muschler et al, and Rieser et al. The Leukosorb™ filter of Caplan et al teaches to filter but not culture mesenchymal stem cells. Adding the "culturing" limitation in this application, Caplan et al would teach away from this invention. The material and the purpose of the plate taught by Muschler et al are different from this application. The functions of Rieser et al and this application are also different. Accordingly, this application now should be placed in condition of allowance. An early Notice to this effect is respectfully expected.

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